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Factors associated with preservation of facial nerve function after surgical resection of vestibular schwannoma

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Abstract Avoidance of facial nerve palsy is one of the major goals of vestibular schwannoma (VS) microsurgery. In this study, we examined the significance of previously implicated prognostic factors (age, tumor size, the extent of resection and the surgical approach) on post-operative facial nerve function. We selected all VS patients from prospectively collected database (1984–2009) who underwent microsurgical resection as their initial treatment for histopathologically confirmed VS. The effect of variables such as surgical approach, tumor size, patient age and extent of resection on rates facial nerve dysfunction after surgery, were analyzed using multivariate logistic regression. Patients with preoperative facial nerve dysfunction (House-Brackman [HB] score 3 or higher) were excluded, and HB grade of 1 or 2 at the last follow-up visit was defined as “facial nerve preservation.” A total of 624 VS patients were included in this study. Multivariate logistic regression analysis found that only pre-operative tumor size significantly predicted poorer facial nerve outcome for patients followed-up for ≥ 6 and ≥ 12 months (OR 1.27, 95% CI 1.09–1.49, $p < 0.01$; OR 1.35, 95% CI 1.10–1.67, $P < 0.01$, respectively). We found no significant relationship between facial nerve function and age, extent of resection, surgical approach, or tumor size (when extent of resection and surgical approach were included in the regression analysis). Because facial nerve palsy is a debilitating and psychologically devastating condition for

the patient, we suggest altering surgical aggressiveness in patients with unfavorable tumor anatomy, particularly in cases with large tumors where overaggressive resection might subject the patient to unwarranted risk. Residual disease can be followed and controlled with radiosurgery if interval growth is noted.

Keywords Vestibular schwannoma · Acoustic neuroma · Microsurgery · Facial nerve function · Facial nerve palsy

Introduction

Vestibular schwannoma (VS) is a benign tumor that arises from one or more constituent nerves comprising the eighth cranial nerve complex [1, 2]. Attempts at surgical removal of these tumors can be complicated by intraoperative damage to the facial nerve and the cochlear nerve, along with other neurological and vascular injuries [1, 3–13]. Even though advances in surgical techniques have improved facial nerve outcomes, functional preservation is still an issue because injury to the facial nerve has significant physical and psychological consequences for the patient [14–16]. It has been suggested that age, tumor size, and surgical approach all can impact ultimate facial functional outcome [16–19].

There are a number of studies in the literature that present the outcome of facial nerve function after VS resection; however, these studies largely are small to modest sized case series [12]. In this study, we prospectively collected facial nerve function data on 624 patients over a course of 25 years. We examined the significance of previously implicated prognostic factors (age, tumor size, the extent of resection and the surgical approach) on the rates of post-operative facial nerve preservation.

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Methods

Patient population

Clinical, radiographic and audiometric data for all patients evaluated and/or treated for a known or presumed VS by the senior authors (Lawrence H. Pitts and Andrew T. Parsa) at our institution over a 25 year period (1984–2009) were prospectively collected in a database. We retrospectively identified all patients in this database with data relevant to this study undergoing microsurgical resection of VS. Patients with a history of prior microsurgery for VS, or radiosurgery/radiotherapy were excluded. Also, any patient who did not have 6 months of follow-up, including early post-operative death, were excluded from analysis. This study was conducted with the approval of the University of California at San Francisco Committee on Human Research under approval number H41995-32911-01.

Data analysis

Patient data were collected prospectively. In all cases, intraoperative direct stimulation of the tumor surface, monitored by facial EMG, was used to identify the facial nerve position and function prior to any tumor manipulation and resection. Permanent facial nerve dysfunction was defined as House-Brackman (HB) grade 3 or higher function persisting for greater than 6 months beyond the date of surgery [20].

Tumor size was measured as the largest single pre-operative tumor diameter including the intracanalicular portion. The extent of resection was judged by subjective intraoperative impression; however, if an MRI performed within 6 months of surgery demonstrated that this impression was wrong, the extent of resection classification was reclassified to correlate to the MRI findings. Near total resection (NTR) indicates that only of a thin layer of tumor remained on one or more nerves in a conscious attempt to preserve function. If imaging studies revealed gross evidence of residual disease, then it was termed subtotal resection (STR).

Statistical analysis

In this study, we assessed the relationship between permanent facial nerve palsy and age, tumor size, the extent of resection and the surgical approach. Binary variables were compared using Pearson's χ^2 test. Continuous variables were compared using an independent samples *t*-test or ANOVA.

Given statistically significant between group differences in potentially confounding variables, such as tumor size, we performed multivariate regression analysis to study the

impact of tumor size, extent of resection, and surgical approach on facial nerve function. Variables which impacted facial nerve outcome with a $P = 0.2$ or less on univariate analysis were included in stepwise binary logistic regression modeling [21]. All odds ratios on multivariate analysis, reflect the risk of having facial nerve palsy at 6 month post-operatively. The goodness of fit of the regression model was confirmed by demonstrating a non-significant P -value on the Hosmer–Lemeshow test [21, 22].

We tested interaction terms between each of the three variables to significantly impact hearing on univariate analysis. The statistical significance of the interactions was assessed with the use of backward stepwise regression, in which statistical significance was estimated by means of the likelihood-ratio test to assess the effect of removing interaction terms for all strata of the given variable [21]. After finding that none of the interaction terms would significantly (unadjusted $P > 0.2$ for all terms) alter the log likelihood of the regression model if removed, we calculated the adjusted odds ratios without adjusting for interactions for ≥ 6 months follow-up and ≥ 12 months follow-up.

Continuous variables are presented as mean \pm SE. Statistical tests were considered significant when the two sided $P < 0.05$ after correcting for multiple comparisons using the Bonferroni method. All statistical tests were performed using SPSS version 17.

Results

Patient population

A total of 624 patients underwent microsurgical resection for acoustic neuroma in this period. About 255 (41%) patients had facial nerve palsy (HB grade 3 or higher) and 369 (59%) patients had normal facial function (HB grade 1 or 2) 6 months post-operatively. The demographic characteristics of these two groups are compared in Table 1. We also present surgeon comparison which shows insignificant relationship to facial nerve preservation (57 vs. 62%, $P = 0.196$; Table 2). The median follow-up for these patients was 37 months, with 64% patients followed ≥ 12 months, 37% patients followed up for > 60 months and 14% of patients followed for > 120 months.

The effect of patient age on facial nerve preservation

The mean patient age was 49.5 years (range 13–80 years) in our study. There was no statistical difference between a patient's age and facial nerve preservation (49 ± 0.79 years for facial palsy vs. 49 ± 0.65 years for normal facial

Table 1 Clinical characteristics of patients in this series

N = 624	Facial nerve palsy		P-value
	Yes 255 (%)	No 369 (%)	
Gender			NS
Male	116 (45)	176 (47)	
Female	139 (55)	196 (53)	
Age (years)	49 ± 0.79	49 ± 0.65	NS
Tumor size (cm)	2.5 ± 0.07	1.9 ± 0.06	<0.0001*
Extent of resection			0.171
Gross total resection	176 (39)	279 (61)	
Near total resection	37 (49)	39 (51)	
Subtotal resection	42 (45)	51 (55)	
Approach			<0.011*
Middle cranial fossa	45 (33)	91 (67)	
Retrosigmoid	58 (36)	103 (64)	
Translabrynthine	152 (46)	175 (54)	
Cyst			NS
Yes	21 (41)	30 (59)	
No	234 (41)	339 (59)	
Neurofibromatosis-2 (NF2)			NS
Yes	15 (50)	15 (50)	
No	240 (40)	354 (60)	

* $P < 0.05$, NS not significant

Table 2 Results of univariate analysis demonstrating the effect of tumor size and surgeon on facial nerve palsy

N = 624	Facial nerve palsy	
	Yes (%)	No (%)
Extracranial tumor diameter (cm)		
≤1.0	24	76
1.1–2.0	37	63
2.1–3.0	48	52
>3.0	56	44
Surgeon		
1	43	57
2	38	62

function, $P = \text{NS}$; Table 1), and this remained an insignificant predictor of outcome in the multivariate model (Table 3).

The effect of size on facial nerve preservation

As expected, the mean tumor size was higher for patients with post-operative facial nerve palsy than for those with normal facial nerve functioning (2.5 ± 0.07 cm vs. 1.9 ± 0.06 cm, respectively, $P < 0.0001$; Table 1). Given

that there was a statistically significant difference in tumor size between patients who had facial nerve palsy and those with normal facial nerve function, we performed univariate analysis based on three ranges for tumor sizes (Table 2). On multivariate analysis, tumor size predicted facial nerve palsy even when extent of resection and surgical approach were included in the regression model for patients followed ≥ 6 and ≥ 12 months (OR 1.27, 95% CI 1.09–1.49, $P < 0.01$; OR 1.35, 95% CI 1.10–1.67, $P < 0.01$; Table 3a and b, respectively).

The effect of extent of resection on facial nerve preservation

Gross total resection (GTR) was performed in 455 (73%) of 624 patients, NTR was performed in 76 patients (12%), and STR was performed in 93 patients (15%). There was no statistical difference ($P = 0.171$) between extent of resection and facial nerve preservation (Table 1) on univariate analysis, and NTR and STR did not alter facial nerve outcomes when tumor size was included in the multivariate regression model for patients followed ≥ 6 and ≥ 12 months. Similarly, GTR was not associated with increased facial nerve palsy when controlling for tumor size.

The effect of surgical approach on facial nerve preservation

The middle cranial fossa approach was performed in 136 (22%) of 624 patients, the retrosigmoid approach was performed in 161 patients (26%), and the translabyrinthine approach was performed in 327 patients (52%). There was no statistically significant relationship ($P = 0.010$) between the surgical approach and facial nerve palsy on either univariate (Table 1) or multivariate analysis for patients followed ≥ 6 and ≥ 12 months.

The learning curve of facial nerve preservation

Table 4 depicts facial nerve preservation rates as a function of year of neurosurgeon experience. As seen in Table 4, that while between-year rates of facial nerve palsy vary significantly, in general, facial nerve preservation were lower in the first 2 years of VS surgical practice, and improved slightly over time.

Discussion

The risk of facial nerve palsy after microsurgical removal of VS cannot be entirely eliminated, even with refinements in surgical technique. Thus, surgical resection of these

Table 3 (a) Results of the multivariate analysis demonstrating the odds ratio and confidence intervals for rate of facial nerve palsy when tumor size, extent of resection and surgical approach are included in the regression model facial outcomes at 6 months and (b) multivariate analysis limited to facial outcome at 12 months

	OR	Facial nerve palsy 95% CI		<i>P</i> -value
		–	+	

(a) ≥ 6 months follow-up (<i>N</i> = 624)				
Tumor size (cm)				
Per 0.1 cm	1.27	1.09	1.49	<0.01
Extent of resection				
Near Total resection	1.23	0.71	2.17	0.70
Subtotal resection	1.05	0.66	1.67	1.19
Surgical approach				
Retrosigmoid	0.80	0.66	1.14	0.19
Translabyrinthine	1.04	0.66	1.64	1.14
(b) ≥ 12 months follow-up (<i>N</i> = 400)				
Tumor size (cm)				
Per 0.1 cm	1.35	1.10	1.67	<0.01
Surgical approach				
Retrosigmoid	0.93	0.63	1.36	0.705
Translabyrinthine	0.79	0.55	1.15	0.223

Table 4 Facial nerve outcomes expressed as a function of years of surgeon experience

Surgeon year	<i>n</i>	Percentage facial nerve preservation
1	16	50
2	25	52
3	20	60
4	12	50
5	9	44
6	20	70
7	24	71
8	26	77
9	29	66
10	30	57
11	30	63
12	22	45
13	40	45
14	45	62
15	43	56
16	45	51
17	47	53
18	51	63
19	36	64
20	31	71
21	23	65

tumors is associated with significant risk of physical, cosmetic, and psychological morbidity associated with significant facial nerve palsy [8, 23]. Previously, in a systematic review of the literature, we focused on factors associated with reported rates of facial nerve function in a

large population of 11,873 patients treated VS, and found that patients with larger tumors were less likely to have preserved facial nerve function after surgery than patients with smaller tumors (≤ 2.0 cm 90% vs. >2.0 cm 67%, $P < 0.0001$) [12].

In this study, we examined facial nerve function in 624 patients undergoing VS surgery at our institution and found that tumor size is the most important predictor of facial nerve outcome, and that age, extent of resection and surgical approach do not independently predict facial palsy. This finding replicates the results of our previous systemic review.

The facial nerve can usually tolerate a large degree of stretching, compression or distortion without apparent facial palsy [19, 24]. However, as the tumor grows, the nerve comes under even greater tension, which increases the likelihood of stretch injury, and this may explain the high rate of facial palsy seen in patients with large tumors [19, 24]. Facial nerve dysfunction may also result from poor vascularization of nerve segments that are effaced by large tumors [19, 24]. While larger tumors pose greater risk to the nerve; however, tumor size alone cannot predict the degree of adhesiveness, or the difficulty of dissection [18, 19], suggesting that other factors also impact facial nerve outcome. The facial nerve can traverse any part of the tumor capsule and even pass through the tumor itself, a feature that occurs equally in small and large tumors [15]. Thus, additional methods for pre-operative assessment of these patients may be needed to improve surgical outcomes.

The lack of benefit we observed with less aggressive resection deserves additional discussion. Our STRs were not planned, and it is interesting to speculate that an approach of intentional STR might be warranted in many

cases. The concept of intentional STR or STR based on intra-operative findings might represent the future of VS surgery, and is certainly worthy of further study. The cases that were subtotal or NTR relate to factors such as thinning of the facial nerve or adherent vessel loops that preclude safe removal of tumor. Thus, while our data do not prove hypothesis that STR of large VS is superior to GTR, our consideration of these findings have changed our practice, and led us to plan STR's in more difficult cases, stopping earlier, and treating the residual fragment with radiosurgery post-operatively. Time will tell whether this is the best way to improve facial nerve outcomes in these patients.

Further, while there may be a small difference in facial nerve outcomes between patients receiving GTR and STR, our analysis suggests that it may take a large study to demonstrate this benefit. We performed a power analysis and found that to demonstrate the 8% between group difference demonstrated in this study with 80% power and $\alpha = 0.05$ would require 454 patients per group. We think such an effort would take several centers many years to demonstrate.

In conclusion, because facial palsy is a debilitating and psychologically devastating condition for the patient, we suggest altering surgical aggressiveness in patients with unfavorable tumor anatomy, particularly in cases with large tumors. It has been shown in the literature that neuro-monitoring during VS resection can be an effective approach to preserve facial nerve function, although it has limited ability to predict the extent or rate of recovery in cases of abnormal function [14, 25–28]. With large tumors, residual disease can be followed and controlled with radiosurgery if interval growth is noted [3, 15].

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